Supporting Information

Supplementary Figure I. Full survey questionnaire.

Survey: Perspectives on Storage of Blood Used for Transfusion

Your answers to the following questions will determine whether you are eligible to participate in this survey.

a. Does your current position involve clinical, scientific, or administrative aspects related to blood transfusion and/or the care of patients requiring blood transfusion?

- O Yes
- O No (see ineligibility statement)

Ineligibility statement: If you answered NO to this question, your current position is not directly related to the study; therefore, please do NOT complete the survey.

b. Have you already completed a similar survey on blood storage and rejuvenation at the Biomet booth or as part of a workshop during this AABB conference?

- O Yes (see ineligibility statement)
- O No

Ineligibility statement: If you answered YES to this question, your responses have already been collected; therefore, please do NOT complete the survey.

1. Your **primary** role associated with blood transfusion: (select one)
   - O Collecting blood
   - O Supplying blood
   - O Ordering blood
   - O Conducting transfusions
   - O Providing care to patients requiring transfusions
   - O Other; please specify _____

2. Your **primary** function in relation to transfusion medicine: (select one)
   - O Administrator
   - O Clinician
   - O Technician
   - O Laboratory Director/Transfusion Medicine Physician
   - O Other; please specify _____

3. Approximate number of years working in transfusion medicine:
   - ____ years

4. Type of institution where employed: (select one)
   - O Blood center (non-hospital based)
   - O Hospital
   - O Outpatient center
   - O Other; please specify _____

With the use of additive solutions, the FDA allows RBCs to be stored for up to 42 days.

5. Based on available scientific evidence, in your opinion, what is the appropriate duration limit for RBC storage prior to transfusion?
   - ____ days

6. To the best of your ability, please estimate the average age (in days) of RBC units transfused at your institution:
   - ____ days
   - O Don't know
   - O Not applicable

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Please use the following scale to indicate your level of agreement with the following statements:

1. Strongly disagree 2. Disagree 3. Agree 4. Strongly agree

7. When fresher RBC units are used, less blood is needed for transfusion

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

8. Well-designed, adequately powered, controlled, randomized trials are needed to answer questions about the impact of blood storage on patient outcomes

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

9. Most institutions are not pursuing measures to reduce the age of stored blood at time of transfusion

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

10. I am aware of guidelines published by AABB that aim to reduce the number/volume of blood transfusions as appropriate

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

11. If fewer units were required to treat each patient requiring blood transfusion, there would be cost savings for most institutions

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

12. Each unit of blood transfused is associated with additive risk of adverse events

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

13. Clinicians frequently request "fresh" RBCs for transfusion

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

14. Duration of blood storage prior to use is a major concern among transfusion medicine professionals

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

15. I do not believe there is a need for greater scrutiny of the quality of blood used for transfusion in terms of RBC viability and O_2 transport capacity

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

16. A restrictive transfusion threshold (hematocrit 7.0-8.0 g/dL) should be used for the vast majority of hospitalized, stable patients without evidence of inadequate tissue oxygenation

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

17. There is a clear need for increased awareness about the implications of the age of transfused blood on quality of care

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

18. The research does not consistently demonstrate that blood transfusions have worse outcomes using older stored RBCs when compared with fresher blood

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

19. I am confident in the US healthcare system's ability to deliver an adequate quantity of fresh blood

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

20. I would be interested in seeing clinical data that show whether restoring levels of 2,3-DPG to those in fresh blood improve transfusion outcomes.

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

21. Current efforts to reduce costs associated with transfusion medicine focus primarily on conservation (ie, decreasing the number of transfusions/units transfused)

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

22. I am not aware of any commercially available, FDA-approved, in vitro RBC rejuvenation product

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

23. Transfusion-associated infections and overall morbidity increase with the volume and number of blood transfusions given to a patient

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

24. Treating physicians are generally unaware of changes that occur over time in stored RBCs

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

25. I believe that minimizing or reversing the changes that occur over time in stored RBCs may impact the clinical benefits of blood transfusions

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

26. I have not observed an overall increase in efforts to improve the quality of blood stored for transfusion

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

27. Restoring 2,3-DPG and ATP levels to those in fresh blood is a promising approach to reducing the number of RBC units required for transfusion

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

28. The parameters that currently define the acceptable duration of RBC usability do not consider the capacity of stored RBCs to effectively deliver O_2 to tissues

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

29. I believe that transfusion of RBCs with depleted 2,3-DPG and ATP may impact the clinical benefits of blood transfusion

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

30. Restoring 2,3-DPG and ATP levels to those in fresh blood is a rapid and inexpensive process that can readily be integrated into the transfusion service workflow

STRONGLY DISAGREE 1 2 3 4 STRONGLY AGREE

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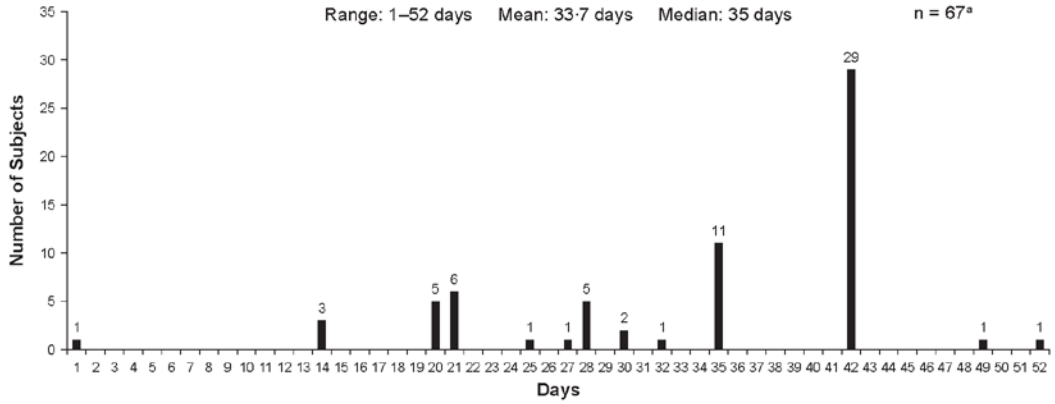
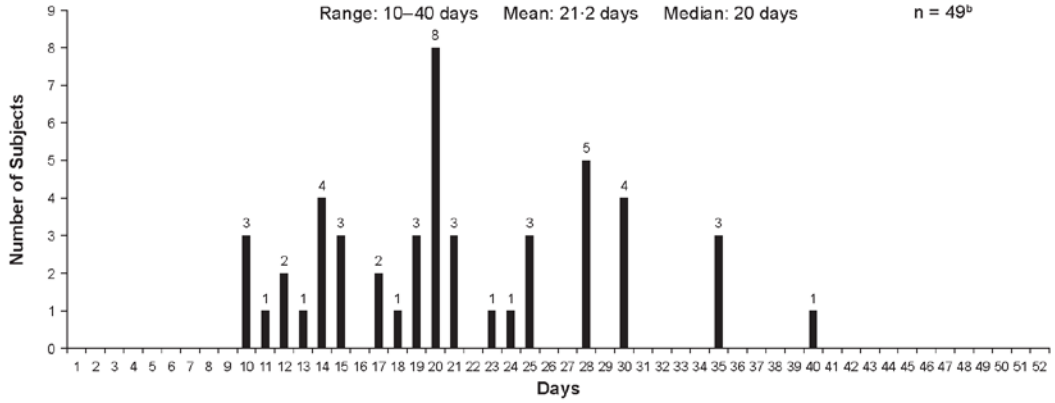
Supplementary Figure II.

A. Appropriate RBC storage limit prior to transfusion, in days, according to participant opinion.



B. Estimated average age of RBC units transfused at participants' institutions, in days.



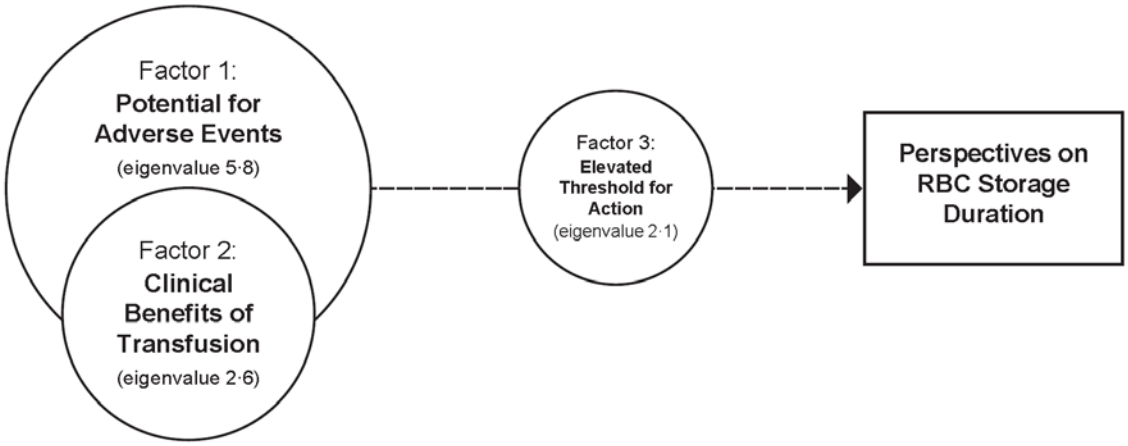
[a]Missing response: n = 2. [b]Don't Know: n = 7; Not Applicable: n = 11; missing response: n = 2.

Supplementary Figure III. Full listing of participant agreement with 24 statements related to RBC storage and its impact on blood quality and transfusion outcomes.

Statements[a]	Agreement[a] (percentage of respondents)	
	Agree	Disagree
When fresher RBC units are used, less blood is needed for transfusion (n = 60)	43·3	59·7
Well-designed, adequately powered, controlled, randomized trials are needed to answer questions about the impact of blood storage on patient outcomes (n = 64)	93·7	6·3
Most institutions are not pursuing measures to reduce the age of stored blood at time of transfusion (n = 64)	81·3	18·7
I am aware of guidelines published by AABB that aim to reduce the number/volume of blood transfusions as appropriate (n = 64)	89·1	10·9
If fewer units were required to treat each patient requiring blood transfusion, there would be cost savings for most institutions (n = 63)	93·7	6·3
Each unit of blood transfused is associated with additive risk of adverse events (n = 64)	92·2	7·8
Clinicians frequently request "fresh" RBCs for transfusion (n = 63)	41·3	58·7
Duration of blood storage prior to use is a major concern among transfusion medicine professionals (n = 63)	65·1	34·9
I do not believe there is a need for greater scrutiny of the quality of blood used for transfusion in terms of RBC viability and oxygen transport capacity (n = 64)	25·0	75·0
A restrictive transfusion threshold (hematocrit 7·0–8·0 g/dL) should be used for the vast majority of hospitalized, stable patients without evidence of inadequate tissue oxygenation (n = 64)	82·8	17·2
There is a clear need for increased awareness about the implications of the age of transfused blood on quality of care (n = 64)	82·8	17·2
The research does not consistently demonstrate that blood transfusions have worse outcomes using older stored RBCs when compared with fresher blood (n = 64)	79·7	20·3
I am confident in the US healthcare system's ability to deliver an adequate quantity of fresh blood (n = 63)	55·6	44·4
I would be interested in seeing clinical data that show whether restoring levels of 2,3-DPG to those in fresh blood improves transfusion outcomes (n = 64)	89·1	10·9
Current efforts to reduce costs associated with transfusion medicine focus primarily on conservation (ie, decreasing the number of transfusions/units transfused) (n = 64)	90·6	9·4
I am not aware of any commercially available, FDA-approved, in vitro RBC rejuvenation product (n = 61)	55·7	44·3
Transfusion-associated infections and overall morbidity increase with the volume and number of blood transfusions given to a patient (n = 64)	87·5	12·5
Treating physicians are generally unaware of changes that occur over time in stored RBCs (n = 64)	84·4	15·6
I believe that minimizing or reversing the changes that occur over time in stored RBCs may impact the clinical benefits of blood transfusions (n = 64)	96·9	3·1
I have not observed an overall increase in efforts to improve the quality of blood stored for transfusion (n = 64)	70·3	29·7
Restoring 2,3-DPG and ATP levels to those in fresh blood is a promising approach to reducing the number of RBC units required for transfusion (n = 61)	83·6	16·4
The parameters that currently define the acceptable duration of RBC usability do not consider the capacity of stored RBCs to effectively deliver oxygen to tissues (n = 62)	87·1	12·9
I believe that transfusion of RBCs with depleted 2,3-DPG and ATP may impact the clinical benefits of blood transfusion (n = 63)	84·1	15·9
Restoring 2,3-DPG and ATP levels to those in fresh blood is a rapid and inexpensive process that can readily be integrated into the transfusion service workflow (n = 61)	57·4	42.6

[a]Statements are listed in order of appearance on the survey questionnaire. [b]Responses have been dichotomized into agree and disagree from the original 4-point scale (strongly agree, agree, disagree, strongly disagree).

Supplementary Figure IV. Exploratory factor analysis was performed on all surveys with complete data (n = 56) using principal component methodology. Eight factors were identified with eigenvalues ≥1, accounting for 70·7% of the total observed variability in the data. Of these, the 3 factors with the greatest eigenvalues (all >2) represented themes clearly related to blood storage duration and evident in the literature; these were included in this final principal component model illustrating how the potential for adverse events, the clinical benefits of transfusion, and an elevated threshold for taking action with respect to RBC storage all interact to influence participants' perspectives on RBC storage duration.



Supplementary Table I. Survey items contributing to each of the 3 main factors identified by principal component analysis.[a]

Factor/Theme (eigenvalue)	Contributing Survey Items (factor coefficient)
Potential for Adverse Events (5·8361)	Each unit of blood transfused is associated with additive risk of adverse events (0·73497)
	I believe that minimizing or reversing the changes that occur over time in stored RBCs may impact the clinical benefits of blood transfusions (0·72810)
	The parameters that currently define the acceptable duration of RBC usability do not consider the capacity of stored RBCs to effectively deliver O_2 to tissues (0·70555)
	I am aware of guidelines published by AABB that aim to reduce the number/volume of blood transfusions as appropriate (0·65526)
	Treating physicians are generally unaware of changes that occur over time in stored RBCs (0·64986)
	I believe that transfusion of RBCs with depleted 2,3-DPG and ATP may impact the clinical benefits of blood transfusion (0·63954)
Clinical Benefits of Transfusion (2·5685)	When fresher RBC units are used, less blood is needed for transfusion (0·61072)
	Restoring 2,3-DPG and ATP levels to those in fresh blood is a rapid and inexpensive process that can readily be integrated into the transfusion service workflow (0·55503)
	I believe that transfusion of RBCs with depleted 2,3-DPG and ATP may impact the clinical benefits of blood transfusion (0·49486)
	The research does not consistently demonstrate that blood transfusions have worse outcomes using older stored RBCs when compared with fresher blood (–0·48904)
	Treating physicians are generally unaware of changes that occur over time in stored RBCs (0·46966)
	Restoring 2,3-DPG and ATP levels to those in fresh blood is a promising approach to reducing the number of RBC units required for transfusion (0·44227)
Elevated Threshold for Action (2.1391)	I am not aware of any commercially available, FDA-approved, in vitro RBC rejuvenation product (0·56674)
	Duration of blood storage prior to use is a major concern among transfusion medicine professionals (–0·55105)
	Most institutions are not pursuing measures to reduce the age of stored blood at time of transfusion (0·50909)
	Restoring 2,3-DPG and ATP levels to those in fresh blood is a promising approach to reducing the number of RBC units required for transfusion (0·47602)
	I have not observed an overall increase in efforts to improve the quality of blood stored for transfusion (0·43684)

[a]Three additional factors/themes not included in the final model (with eigenvalues ≥1 and <2) were blood conservation strategy (1·6), RBC storage duration linked to RBC quality (1·4), and rejuvenation acceptance (1·2).